Remarks

Claims 1, 2, 9-11 and 38-42 are pending in the subject application and currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

As an initial matter, Applicants gratefully acknowledge the Examiner's withdrawal of the previous rejection under 35 U.S.C. § 102 and the obviousness-type double patenting rejection over Remenar *et al.* Although the obviousness-type double patenting rejection over Remenar *et al.* (U.S. Patent No. 7,078,526) is withdrawn on page 4 of the Office Action, the rejection remains on page 12. The Examiner indicated during a telephonic interview on December 27, 2007 that the rejection was an error and that no response was required. Applicants also acknowledge the Examiner's indication that claims 1, 2, 9-11, and 38-42 are free of the prior art.

Claims 1, 2, 9, 10 and 38-42 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Office Action argues that Applicants have shown the formation of particular co-crystals, such as those recited within claim 11, but do not exemplify the formation of all co-crystals containing any solid API and any-co-crystal former that is liquid or solid and where the components are hydrogen bonded to one another or co-crystals with any of the numerous and diverse different co-crystal formers recited in claim 2 or the APIs recited within claim 6. The Office Action also indicates that the specification describes only the preparation of the particular co-crystals recited within claim 11 and does not describe the claimed invention in a manner sufficient to convey that the inventors were in possession of the entire claimed invention, including the formation of co-crystals containing any API and any co-crystal former that are hydrogen bonded. Applicants traverse.

It is incumbent upon the Patent Office to clearly establish that the as-filed specification fails to provide an adequate written description for the claimed invention; the written description of the as-filed specification is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. See, *e.g.*, *In re Marzocchi*, 439 F.2d 220, 224, 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971). In the case of the instant application, Applicants respectfully submit that a *prima facie* case providing reasons why one skilled in the art would not have recognized that the inventors were in possession of the claimed invention has not been established. Rather, the Office Action makes a general allegation that the as-filed specification

fails to provide adequate written description of the claimed invention because the examples do not exemplify or otherwise show the formation of all co-crystals. Applicants also respectfully submit that compliance with the written description requirement does not turn on the number of examples provided in the as-filed specification. Specifically, the Federal Circuit held that examples are not necessary to support the adequacy of a written description and that the written description standard may be met even where actual reduction to practice of an invention is absent. See *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1366, 79 U.S.P.Q.2d 1001 (Fed. Cir. 2006). Accordingly, Applicants respectfully request that the rejection be withdrawn as the grounds articulated for maintaining the rejection are inconsistent with governing law and because the Office Action fails to establish a *prima facie* case that the written description provided by the as-filed specification is insufficient.

Claims 1, 2, 9, 10 and 38-42 are rejected under 35 U.S.C. §112, first paragraph, as nonenabled by the subject specification. The Office Action acknowledges that the specification is enabled for the preparation and use of the particular pharmaceutical co-crystals, but it is not enabled for the preparation of all co-crystals having any API that is solid, and any co-crystal former that solid and liquid, where components are hydrogen bonded to one another, or all co-crystals having the numerous and diverse APIs and co-crystal formers. Thus, the specification fails to provide sufficient support for the broad recitation of a co-crystal composition containing any solid API, in general, with any solid or liquid co-crystal-former, in general, in which the components are hydrogen bonded to each other.

The Office Action states that the application is enabling for the preparation and use of the particular pharmaceutical co-crystals as recited in claim 11, but is not enabling of all co-crystals having any API that is solid, and any co-crystal former that is solid or liquid, where the components are hydrogen bonded to one another, or all co-crystals having the numerous and diverse APIs and co-crystal formers. The Office Action states that the instant specification fails to provide information that would allow the skilled artisan to fully make and use the instant invention without undue experimentation and cites the eight factors identified in *Ex parte Forman*, 230 U.S.P.Q. 546 (Bd. Pat. App. Int. 1986) at 547.

Of the eight factors, the Office Action identifies that the nature of the invention pertains to a

co-crystal composition containing a solid API and a solid or liquid co-crystal former, where the API and co-crystal former are hydrogen bonded to one another. The Office Action identifies that the relative skill of those in the art to be very high, typically having advanced degrees. The Office Action also states the breadth of the claims to be so broad so as to exacerbate the lack of predictability (relating to the use of any API and any solid or liquid co-crystal former) and that the specification does not provide any direction or guidance that is sufficient for one of ordinary skill in the art. Although the Office Action states that the specification provides working examples showing the fabrication of the 32 particular co-crystals recited in original claim 11, it concludes that such examples are not adequate guidance as to how one of ordinary skill in the art could prepare all other crystals containing any API and co-crystal former. Ultimately, the Office Action states that the quantity of experimentation required is considered undue and that one of ordinary skill could not determine the manufacturing conditions required to achieve crystallization or what combinations of APIs and co-crystal formers would even be capable of being recovered in crystal form. In support of its position regarding the unpredictability, the Office Action characterizes the state of the art as being unpredictable due to numerous different crystallization factors needed to be controlled and the unpredictability to predicting the different types of crystals that may exist. Support for this position, it is argued, is supplied by Gavezzotti "Are Crystal Structures Predictable?" (Acc. Chem. Res. 1994, vol. 27, pages 309-14). The Office Action alleges that Gavezzotti indicates that the formation and structure of crystals are unpredictable at best. Applicants respectfully traverse the rejection.

Gavezzotti is a reference published about eight (8) years prior to the priority date for the instant application and has little relevance to the claimed invention. Applicants note that this reference is directed to mono-crystals of compounds rather than co-crystals of the compounds. Additionally, it is respectfully submitted that the cited reference does not accurately reflect the state of the art at the time of the invention was made (e.g., compositions comprising co-crystals of APIs co-crystal formers). Further, the cited reference does not address the considerations and teachings provided in the specification for identifying appropriate APIs and co-crystal formers to be used in making the claimed compositions. In this regard, Applicants note that crystal engineering is an art recognized field related to the rational design of pharmaceutical co-crystals. For example, Almarsson *et al.* (Ref. R114 in the Information Disclosure Statement filed September 21, 2006)

indicates that " ... it has become clear that a wide array of multiple component pharmaceutical phases, so called pharmaceutical co-crystals, can be rationally designed using crystal engineering ..." (see page 1889, column 1, paragraph 1). Thus, it is respectfully submitted that Gavezzotti fails to support the position that making pharmaceutical co-crystals is an unpredictable area.

As the Patent Office is aware, enablement is a legal determination of whether a patent enables one skilled in the art to make and use the claimed invention (*Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 960, 220 U.S.P.Q. 592, 599 (Fed. Cir. 1983)) and is not precluded even if some experimentation is necessary. *Atlas Powder Co. v. E.I. Du Pont De Nemours & Co.*, 750 F.2d 1569, 1576, 224 U.S.P.Q. 409, 413 (Fed. Cir. 1984); *W.L. Gore and Associates v. Garlock, Inc.*, 721 F.2d 1540, 1556, 220 U.S.P.Q. 303, 315 (Fed. Cir. 1983). Additionally, the Patent and Trademark Office Board of Patent Appeals and Interferences has stated: "The test [for enablement] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed". *Ex parte Jackson*, 217 U.S.P.Q. 804, 807 (1982); *see also Ex parte Erlich* 3 U.S.P.Q.2d 1011 (B.P.A.I. 1982) (observing that although a method might be "tedious and laborious," such experimentation is nevertheless "routine" defining "routine" experiments as those which use known methods in combination with the variables taught in the patent to achieve the expected, specific, patented result).

In this case and as noted in the Office Action, the claimed co-crystal compositions are made up of solid APIs and solid or liquid co-crystal formers that are hydrogen bonded. Non-limiting examples of APIs are provided in the as-filed specification in Table 4 and non-limiting examples of co-crystal formers and their functionalities are disclosed in Tables 1 and 2. The as-filed specification also teaches how one skilled in the art is to form the claimed co-crystal compositions (*e.g.*, melt re-crystallization, grinding, milling, standing, solution evaporation, thermally driven crystallization from solution, vapor diffusion, anti-solvents, high throughput crystallization protocols, *etc.*, see, for example, page 14, lines 8-19 and page 43 of the as-filed specification). Thus, Applicants respectfully submit that the as-filed specification provides adequate teaching to one skilled in the art as to how to make the claimed compositions. Furthermore, while it is possible that a considerable amount of

experimentation may be required, Applicants respectfully submit that this experimentation is permissible as it is merely routine and the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed and enables those skilled in the art to practice the invention as claimed. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Claims 1, 2, and 10 are provisionally rejected on the ground of nonstatutory "obviousness-type" double patenting over claims 86-93 of copending Application No. 10/546,963. Claims 1, 2, 9-11, and 38-42 are provisionally rejected on the ground of nonstatutory "obviousness-type" double patenting over claims 1-49 and 72-87 of copending Application No. 10/570,405, over claims 66-72 of copending Application No. 10/551,014, and over claims 2-7, 16, and 18 of copending Application No. 10/926,842. Applicants respectfully request that these rejections be held in abeyance until such time that allowable subject matter is indicated.

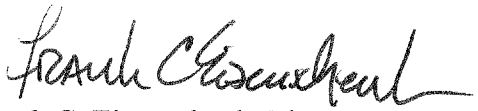
Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



Frank C. Eisenschenk, Ph.D.
Patent Attorney
Registration No. 45,332
Phone No.: 352-375-8100
Fax No.: 352-372-5800
Address: P.O. Box 142950
Gainesville, FL 32614-2950

FCE/sl